A previous assertion of the relation of scleroderma with syphilis would appear to be set aside by the high percentage of negative Wassermann reactions in this group.[18]

In summary this case of scleroderma possesses many features very characteristic of the disease in its usual form. The associated sclerodactyly appears quite typical of those cases previously reported in which radiographic studies of the bones have been made. There is a characteristic atrophy, absorption and eventual disappearance of the terminal phalanges most commonly in the hands and sometimes in the feet.

NEUROCIRCULATORY ASTHENIA (SOLDIERS' HEART).

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If one may judge from the literature on soldiers' heart, this syndrome, the original description of which we owe to Da Costa, has been the most studied of the diseases of the war. The English school of MacKenzie and Lewis early recognized the functional basis of the syndrome and did much to rob the disease of the great terror and fear of impending dissolution with which the lay victims contemplated it. It redounds much to the credit of the school of clinical observation, of which MacKenzie is the great exponent, as opposed to that of abstract scientific analysis, that the tachycardia, breathlessness, murmurs, etc., were not considered in those days indicative of organic changes in the heart. Although definite progress in the treatment of some variety of these conditions has been achieved by the Lewis school, there is no agreement, in our opinion, either in the etiological factors concerned in the causation or the pathogenesis of the syndrome. When the reports on soldiers' heart in the American draft army became available, two very striking facts were apparent:

1. That this condition was not an uncommon symptom-complex of civilian youths, much intensified by the conditions attending the early stages of the draft.
2. That the etiology of these cases did not altogether agree with the etiological factors believed to be responsible for the cases developing on active service.

In reviewing the literature on soldiers' heart, we are forced to ask the question, "Have we quite exhausted, in our analysis of the symptomatology of soldiers' heart, the possibilities in pathogenesis and their relation to the etiological factors believed to be the cause of the condition?" We believe not.

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[18] Osler, Wm.: On Diffuse Scleroderma with Reference to Diagnosis and Use of Thyroid Gland Extract, Jour. Cut. Dis., 1898, xvi, 49 and 127.

Sir James Barr, from 1916, gave us in the literature what he considered sufficient facts to establish the entity of soldiers' heart as hyperthyroidism.

Harlow Brooks, from his study, concluded that the condition was one of hyperthyroidism. Robey and Boas believed the cause to be "a fundamental instability of the patient, that cannot be cured." McFarlane found his group of men had been subjected for many years to a low-grade infection.

Lewis considers infection the predominant etiological factor in the syndrome.

From this array of opinion we are offered three etiological factors: (1) hyperthyroidism, (2) constitutional instability, (3) infection; and we propose to attempt an analysis of these factors in relation to what we believe to be the pathogenesis of the disease.

That the disease was hyperthyroidism is a theory which comes to us supported by such sound clinical judgment as Harlow Brooks in America and Sir James Barr in England, both of whom described in the picture palpable thyroid enlargement as well as the clinical phenomena common to hyperthyroidism. Many other observers agree with this view. Lewis and his school dispose of the theory of hyperthyroidism after failure to demonstrate a more or less constant palpable thyroid enlargement. We believe this inadequate ground for dismissal of the theory: (1) because the personal factor in deciding the presence or absence of thyroid enlargement is a very considerable one, and (2) because no one has, to our knowledge, noted palpable thyroid enlargement as a more or less constant finding among the troops in France; yet McNee and Dunn found the average weight of the thyroid from sixty-five men killed in action 26.7 grams, a figure notably above the normal for civilian males of corresponding age. Again, palpable thyroid enlargement is a doubtful criterion of hypersecretion of the thyroid gland; even in Basedow's disease we have the authority of Murray, that a large percentage of the glands are not noticeably enlarged.

When we leave the debatable ground of thyroid enlargement and approach the symptomatology of the two conditions we see a strong justification for the supporters of the hyperthyroidism theory.

There is a striking similarity in the clinical phenomena of the two conditions, and if we disregard the signs in Basedow's disease known to be due to stimulation of the superior cervical the phenomena are identical. These phenomena are attributable to a hyperirritability of the opposing sets of fibers in the autonomic nervous system, and include the following:

(*a*) Epiphora Loewi 0.5 phenomena; excess or lack of saliva.

(*b*) Asthmatic dyspnea or tachypnea.

(*c*) Tachycardia, pulsus irregularis and respiratorius, vasomotor angina.
  Subjective palpitation. Transitory change in blood-pressure.
  Vasomotor symptoms, especially transitory erythema and dermatographism.

(*d*) Gastrospasm, pylorospasm, gastric hyperacidity, spastic constipation.
  Unmotive watery movements, painless diarrhea, unmotive vomiting.
  Pollipiuria, polyuria, oliguria.
  Profuse sweating. All domain under autonomic control.

There is a growing opinion among students of Graves's disease that we have too long been concentrating our attention on the cardinal triad and too little considering the other phenomena of the disease, and that we have, in the words of Pottinger, been confusing several different entities in our cases of Graves's disease.

The type of Eppinger and Hess, described as sympatheticotonic and characterized by marked exophthalmos, epinephrin mydriasis, Möbius's sign, dry eyes, no sweating, no diarrhea, is a definite entity. These phenomena are attributable to stimulation of the sympathetic fibers whose motor cells lie in the cervical sympathetic, and there is a striking absence of phenomena which lead to the parasympathetic system. For the firm foundation to the pathogenesis of this type we owe much to the researches of the pathological department of the Mayo school, as the following extract from the reports of Wilson and Durant would attest: "It would appear from our examination by the method detailed that definite histological changes do occur in the cervical sympathetic ganglia in hyperplastic toxic (exophthalmic) goitre, and, further, these histological changes consist of various states of degeneration, viz.: (*a*) hyperchromatization, (*b*) hyperpigmentation, (*c*) chromatolysis and (*d*) atrophy of the nerve cells. All these are but successive steps in degeneration, which, if uninterrupted, proceed to the complete destruction of the ganglion cells affected. Not all of the ganglion cells in any of the ganglia examined were so completely destroyed as to render impossible their return to normal, under favorable conditions. There is some evidence that in ganglia, from cases clinically improved, some of the cells have partially or wholly recovered.

After separating cases of this type from the syndrome of Graves's disease we have left a greater group in which the symptomatology is attributable, in great part, to tissues supplied by the autonomic nervous system. Particularly is this so in cases of hyperthyroidism without frank exophthalmos. In such cases, if we except the thyroid increase, all the phenomena may be attributed to hyperactivity of the greater vagus system. It does not appear possible to us that hypersecretion of the thyroid autocoid can explain these striking differences in clinical pictures.

Let us examine the autonomic nervous system. All tissues in the domain of this system have a double innervation. Normally, there is a stable balance between the innervation of one set and the other set of fibers in this system. In both diseases under discussion there is a hyperactivity of both sets of fibers, and the problem in the study of the pathogenesis is the determination of the mechanism and causation of this hyperirritability. It has long been assumed that the autocoid of the thyroid is responsible for the irritability of this system. It was explained that thyroid sensitized or lowered the threshold of these nerve fibers. Recently, considerable doubt has crept into the literature on the subject, as Pottinger's able analysis of the syndrome will show. The supportive proof of thyroid sensitization of any portion of the autonomic system is bound up in the thyroid adrenal interrelation. This is one of mutual stimulation in which the thyroid secretion sensitizes sympathetically innervated tissues to the action of adrenalin; but it is not clear that this action is more than its effect on the pressor fibers in the presence of adrenin. And, again, in weighing this fact we must keep before us that the balance of proof is against there being adrenin in the blood in other but extreme emergency. A much stronger argument against the sensitization theory of the thyroid autocoid is the failure of Levy to demonstrate any effect on the vagus system.

The other commonly accepted explanation of the signs of hyperirritability was that it was due to an adrenalemia. It was believed that a greater than normal outflow of adrenin increased the irritability of the sympathetic fibers, and that, as a result, in attempting to maintain an equilibrium in the autonomic system, a compensatory hyperirritability of the opposing mechanism resulted. This view we believe untenable in the light of our present knowledge. In addition to a stimulation of the tissue supplied by the sympathetic adrenin renders inactive the opposing mechanism. This is illustrated in the musculature of the gut, the bladder and the blood supply of the kidney. Here in the presence of adrenin essential functions may be carried on, but by the action of the autocoid of the pituitary. This requirement of the organism in the presence of adrenin of other autocoids is well illustrated by the part the thyroid plays. Hoskins and McClure show, by a study of the adrenal effect on the arterioles of the body, that the net effect of pure adrenal activity is not a pressor effect on systemic blood-pressure, and the work of Levy demonstrates that the pressor effect formerly accredited to adrenin is realized by the secretion of the thyroid gland which Cannon and Cattell show is mobilized in the blood in the presence of adrenin. There is little opposition to the consensus of opinion among leading endocrinologists of today that adrenin is present in the blood only in states of emergency, and it is a fair deduction from the foregoing discussion that in the presence of the emergency its action is to supplant rather than to support the involuntary nervous system and in the maintenance of an equilibrium, in the absence of involuntary nervous activity, it is supplemented by other autocoids. We do, however, believe adrenin may play a part in precipitating the syndrome, and in such a way as will be analyzed later in the paper.

We believe, from the foregoing comment, that we are justified in the assertion that there is a definite need to search further than the autocoids of the thyroid and adrenal for the cause of the disturbance in the autonomic nervous system, and particularly should this scrutiny be directed to factors operating in the causation of the predominant vagal phenomena. Further, it seems reasonable to consider the thyroid secondary, and in some instance compensatory to a derangement which finds origin in the vegetative nervous system.

The theory that inherited constitutional predisposition is a factor in the development of instability of the autonomic nervous system is undoubtedly on a sound basis. The vagotonic and sympatheticotonic types of individuals described by Eppinger and Hess are familiar to us all, and it is clear that this predisposition determines the predominance of one of the other set of symptoms in the autonomic system in some cases of Basedow's disease. The part that inherited instability plays in the etiology of neurocirculatory asthenia is probably better illustrated in the studies of the American draft army than in any other group of cases. Both the studies of Robey and Boas and Brooks emphasize this point. Among the draft troops the etiology in the cases was uncomplicated by the many factors of active service known to play a part in the causation of the syndrome. While we agree with Robey and Boas in the conclusion that inherited constitutional tendency is a definite factor in the causation of the syndrome, we cannot agree that all cases are attributable to an inherited constitutional tendency, and that they cannot be cured. This understanding of the causation fails to explain the great number of cases that have developed among men who long flourished in good health on active service in France. Oppenheimer emphasizes this, that 39 per cent. of the group studied at Colchester had absolutely negative histories and had given valuable military service before breaking down. It is safe to say that infection may be the determining etiological factor among the greater number if not all the cases developing among men on active service. This brings before us the question of infection as a cause of autonomic nervous instability. In our work with trench fever, which was by far the most common infection in the troops, we found unmistakable evidence of hyperirritability in this system. The men ill with trench fever uniformly evidenced marked vagal phenomena during the febrile and convalescent stages. Approximately 85 per cent. of cases of trench fever recovered promptly after the febrile illness. The remaining number gradually passed through a subacute on to a chronic state of illness, characterized by irregular low-grade fever, varying degrees of splenic enlargement and a group of nervous phenomena characterized by hyperexcitability of the voluntary and involuntary nervous systems, catalogued clinically as neurasthenia and D. A. H. The deduction from a study of these cases is that the infection was responsible, in the first instance, for the vagal phenomena, and with the cure the patient was rid of the organisms. In the second group the deduction was that the persistence of the infection maintained a hyperirritability of the vagus system and that the attempts of compensation in an equilibrium consistent with a lower plane on the individual resulted in the clinical picture of the chronic disease, or what has been called effort syndrome in some instances, neurasthenia in others. That this picture indicates a chronic infection, in which there is a constant outpouring of the toxins, seems established in the experiments detailed in the following cases:

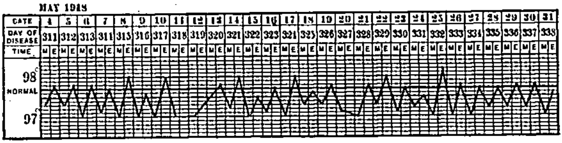

CHART I

CASE 16, aged twenty-eight years, was an A1 man on enlistment, October 12, 1916, and normal during training. To France, April, 1917. On July 5, 1917, he was admitted to hospital with a febrile illness which continued six days and in which he had headache, shin-bone pain and pain in the back. On July 23, 1917, he was invalided to England for pain in the legs, weakness, shortness of breath and giddiness, and during the succeeding months he ran a low grade of fever, with moderate splenic enlargement, chronic muscle and bone pains, especially in the legs, and a progressive nervous instability, with loss of weight and strength. The following is a note of his condition taken from his chart: "Very shaky; sweats freely; flushed face; acute pains in shins; pulse irregular. At night wakes; 'has to fight for breath;' very nervous; sleeps poorly; depressed; frontal headache; breathless on slight exertion; at times dizzy." This is a usual picture of his condition throughout nine months during which he was under observation and in which little result in treatment was realized. In April, a year after his infection, although under hospital care practically the whole time, he presented the picture of a very marked case of neurocirculatory asthenia in which "neurasthenic symptoms predominated."

On the evidence of an eminent authority on neurology this case was transferred to a special hospital under the care of specialists in this branch and returned with a diagnosis of classical neurasthenia.

Clean lice were then fed upon this man throughout the period of the above chart, and following this the excreta from these lice was rubbed into a healthy volunteer who, in the normal incubation period of eight days, developed trench fever. To confirm the experiment further, healthy lice were fed upon the first volunteer who contracted the disease, and by means of their excreta successful transmission to another healthy volunteer was effected.

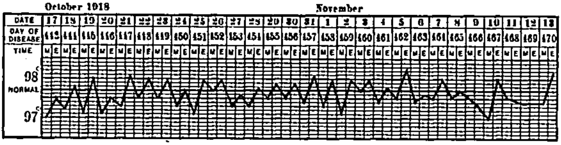

Chart II.

Case 889, aged twenty-three years, enlisted December 27, 1914; went to France in August, 1915. During training was perfectly fit. Carried on full active duty in France until August, 1917, when he began a febrile illness, with shin-bone pain; pain in back; stiffness of ankles and knees; chills; giddiness. After hospital treatment in France and England he attempted light duty. During the year subsequent he was chronically invalided; in June he was in hospital with a febrile relapse. In September, 1918, he was admitted to the New End Military Hospital with a temperature of 102°; dyspnea; palpitation; giddiness; marked nervousness; frontal headache; shin-bone pain; pain in loins, knees and around ankles; eyes pink; notices he gets worried by trifles; feels depressed without cause; occipital headache constant but of varying severity; heavy over eyes; giddiness.

Jan. 1, 1919. Tâche active red; extrasystoles many, one minute after pulse test; complains of marked depression; lack of interest in life; frontal headache; aching in back of neck; sleeplessness, due to itching of skin; urticarial condition.

Jan. 30, 1919. Breathlessness on exertion since first attack of trench fever; loss of concentration; disinclination to do; effort syndrome poor; marked respiratory rhythym to pulse (sinus irregularity). Extrasystoles after exercise; marked fall in pulse volume in deep breathing.

Lice were fed upon this man during the period of the disease indicated by the above chart and the disease successfully transmitted to a healthy volunteer.

Now let us attempt to find an explanation for the vagotonic phenomena in infectious diseases. Probably the most recent and ingenious theory of disease is founded on Vaughan's experiments. He showed that any kind of fever could be produced and maintained for weeks by regulating the size and frequency of dosage of protein. The basis of this is anaphylaxis, in which the parenteral reception of foreign proteins so modifies the cells of the body as to develop a special proteolytic capacity for that particular protein, the process of sensitization. This capacity for specific proteolysis is later exercised at a rate and in a degree to produce toxic substances and certain definite clinical phenomena. The exact composition of these toxins is not known. It is believed that histamin is one of them. Their chief influence is exerted in their action on the vagus system or the muscles supplied by it (Schultz). They therefore closely resemble pilocarpin and the other class of vagus irritants. Histamin, pharmacologically, is in the same class as physostigmin, muscarin and cholin and the like, according to Smith. He traces out the action of pilocarpin and the action of anaphylatoxins in two parallel lines, as follows: If pilocarpin is administered to an individual already showing a tendency to vagus excitability a more marked effect is produced than is obtained when the same dose is administered to a normal individual. When we administer antitoxin for diphtheria to the same type of individual, the vagotonic, we may irritate the vagus system to the point of death, whereas a normal individual is only slightly affected, if at all. Not all vagotonics, however, are susceptible to this exaggerated reaction to horse serum. If one vagotonic reacts to horse serum with symptoms of anaphylactic shock while another does not, manifestly the vagotonic does not in itself determine the response, and a constitutional inferiority of the nervous system does not explain the reaction. The classification of this hyperacute form of serum sickness as an anaphylactic manifestation is not questioned any longer, and the individual displaying it is regarded as sensitized to horse serum. When the shock is survived an anti-anaphylactic state has been observed in some instances. The question may therefore well be asked: "Is not vagotonia in these cases itself an expression of an anaphylactic state, which becomes acute under a specific toxic influence, the same sensitization and previous milder intoxications accounting for the hitherto milder expression of vagotonia?" If such be the case then these phenomena bear a close relationship to the experimentally induced protein fever of Vaughan. The chronicity of the period of sensitization which must be assumed in the vagotonic cases is approximately in Vaughan's experiments.

Smith submits some very substantial evidence that vagotonia, seen clinically, is due to a toxin acting like pilocarpin and histamin, which he considers in most cases an anaphylatoxin. The evidence is set down under the three following headings: (*a*) The closeness of the clinical analogy to experimental anaphylaxis; (*b*) the reasonableness of a protein antigen to play the part of sensitizer and intoxicant under anaphylactic conditions; (*c*) the possibility of demonstrating in the blood antibodies lytic to the suspected protein or in the tissue a specific reactivity.

Certainly, Smith presents a strong array of facts justifying his conclusion of the infectious origin of vagotonia. When we go further and apply this theory to hyperthyroidism and consider that the beginning may be in a parasympathetic hyperirritability, due to a toxin, we find others more or less of the same opinion. As common a disease as tuberculosis is generally recognized to be in large part an anaphylactic disease. Vagotonic phenomena are a prominent feature in the clinical picture. The resemblance of the toxic types of tuberculosis to hyperthyroidism is strongly emphasized by many authorities who note with what great difficulty the differential diagnosis of one from the other may be made. Crile is authority for the statement that, excepting the lesion itself, the postmortem findings in tuberculosis are indistinguishable from those of Graves's disease, and in spite of opinions to the contrary, as preëminent an authority as Pottinger supports the toxemic theory, as the following quotation shows: "I realize that scientific opinion of today is toward the theories that insufficient iodin being obtained by the individual and that of infection being the causative factors in the enlargement of the thyroid gland, but I cannot help but think that a hyperplasia of the gland takes place in the presence of toxemia while no infection of the gland itself occurs." He believes that the hyperirritability in the autonomic system is attributable to thyroid sensitization, the thyroid hypersecretion in turn by increased adrenin in the blood. We believe the evidence is against thyroid sensitization of the vagal fibers in the system and against the adrenal hyperactivity under such conditions.

Clinicians who have followed the work of Lane and his school cannot help but be impressed with the part played in the etiology of hyperthyroidism by material from the large gut. McGarrison's work in this connection is of extraordinary interest. Not uncommonly the teeth, the tonsils and the accessory sinuses have been established as the determining factor, and while admitting the possibility of reflex irritation through the nerve trunks to either the cervical sympathetic or the gland itself, one leans rather to the belief that the chronic infection is the cause. From the foregoing discussion it seems reasonable to conclude that infection, in a great many instances, may be the determining factor in the development of hyperthyroidism, and that many cases of neurocirculatory asthenia have an analogous pathogenesis.

And now let us consider the part the thyroid plays. We know that thyroid secretion follows upon the discharge of adrenin into the blood. This seems firmly established by the work of Cannon. It therefore is active in fright, fear and like sudden emotional states, but that it is transitory and passing with the emergency, when so induced, seems likely, as is the case with adrenin the activator.

Another cause that would seem established is that of primary stimulation in disease of the cervical sympathetic as described by Wilson and Durant. But both causes are operable only in a small group of cases in the syndrome, and we believe there is still a large unexplored field to be worked in establishing the etiology in the disease. Hence, the following facts about a factor we believe of considerable importance.

Barr maintained that the syndrome occurring among the troops in France, which he believed to be hyperthyroidism, was due to a vicious circle in which the deficiency of calcium in the blood was a contributory cause in the production of the hyperthyroidism and the excessive action of the thyroid the cause of a greater calcium metabolism. When we consider that the minimum of calcium per day required for the normal human nutrition is 0.45 gram, and that in the absence of milk from the dietary pounds of meat or common milled cereals would be required to furnish it, the conclusion is justifiable that the fighting units fail to realize their calcium need. Since the time of Besredka it has been known that calcium salts prevent the appearance of anaphylactic phenomena when toxic doses of anaphylatoxin are simultaneously given with the calcium. Burridge has shown that the capacity of tissue activity to compensate inhibition is in direct ratio to its calcium contents. The assumption seems reasonable that deficiencies of calcium in the system require increased thyroid activity in order to liberate calcium from the storehouses. This seems undoubtedly true in view of the established fact that under all contingencies of diet and activity the calcium concentration of the blood is maintained at extraordinarily constant levels and that a greater need for calcium exists in the presence of diseases with which anaphylaxis is a part, this mobilization of calcium compensating inhibitory phenomena in tissue and allowing approximately normal activity.

And now we propose to indicate the relative degree of responsibility of the different factors we believe to be acting in the causation of the syndrome of soldiers' heart.

Two classes of individuals developed the syndrome: (1) the men who, after successfully passing the draft board examination, manifested the syndrome after reaching camp, a result, it would seem, of the nervous and emotional strain of ordinary military service; (2) men exposed to the rigors of active service who manifested the syndrome, and in a great number the onset was fairly sudden, developing in men who had carried on in perfect fettle, in some instances for as long as two or three years before breaking down. Two deductions seem justifiable from these facts that in the individual of potential autonomic instability (neurocirculatory asthenia) the nervous and emotional strain of military service will probably promptly precipitate a syndrome, and that in a normal man factors other than the strain of service are necessary to develop the potentiality.

As an explanation of the manner in which emotional stress and strain act as a cause in the syndrome we have the work of Cannon. He demonstrated in the animal adrenin mobilization in considerable amounts in such states, and it has long been accepted that adrenin acts upon the autonomic nerve structures. We agree that adrenin effect probably explains in part the sensitization of this system in the soldier. But that it is the single factor concerned we somewhat doubt. It would seem probable that profound inhibition in states of fear in the soldier combine with adrenin effect in sensitizing the autonomic system. The training toward and realization of perfect discipline in the soldier is in great part to establish the ascendancy of inhibition from the higher centers over just such primary impulses as those with which adrenin mobilization is concerned.

It would seem probable then that the common state of men in active combatant areas was one of fear, in which the autonomic nervous system was subjected to showers of adrenin and at the same moment profound inhibitory impulses from the brain. An illustration of this may be drawn in that of a spirited horse that at the same moment is locked into inaction by strapping or a tight rein and is cut deeply with a whip.

Another phase in the problem concerned with the understanding of the pathogenesis of functional disease in the soldier, which we believe had been too little considered, is the disturbance of tissue chemistry which we may discuss in terms of calcium metabolism. Gaskell and Elliott, after destruction and degeneration of the nerves of the vegetative system to a part, have demonstrated, after six weeks, full adrenin effect on the part. This would seem to establish adrenin action as directly on the tissue and independent of the vegetative system itself.

Burridge establishes from his experiments that the action of adrenin is to make the tissue independent of its media, particularly the calcium concentration in the prefusing media. Maximum heart work was maintained on a perfusing solution containing one-twelfth the required calcium content when adrenin was added to the solution.

These facts would suggest that individuals living for any time under conditions, such as emotional stress, which tended to a maintenance of relatively high amounts of adrenin in the blood would very soon have an unbalanced tissue chemistry. These facts would explain how the soldier on an abnormally low calcium diet would appear to maintain a calcium equilibrium, and only with the development of sudden call for more calcium, as in acute disease, would we expect manifestations of deficiency.

We believe, therefore, that there is considerable ground for the opinion that some of the phenomena of disease among soldiers, notably the bone pains, tremors thought to be cerebral in origin and general exaggerated response to normal stimuli are an expression of the disorganization of the inorganic chemistry.

However much there is a disagreement on the mechanism of the forces acting in the production of the syndrome neurocirculatory asthenia in what we may call the potential individual at the present moment, we are more concerned with the factors which result in the potentiality, because in our case of the civilian we must be prepared to recognize in its incipient and mild types what has undoubtedly been a very common condition classified under varieties of neurosis, and we believe infections to be the predominant factor in causation of the potentiality. This is the point we wish particularly to emphasize in this paper and consider the other points of interest here only in so far as they support this belief.

CONCLUSIONS. 1. That some types of hyperthyroidism are analogous to the entity neurocirculatory asthenia and their pathogenesis is probably identical, the phenomena being attributable to a hyperexcitability of the opposing sets of fibers of the autonomic nervous system.

2. That in both conditions the syndrome develops in individuals in whom there is a hyperirritability of one or other sets of fibers in the autonomic system. Hence, constitutional predisposition due to inherited sympathetic or vagotonic instability is a factor in the causation on a sound basis.

3. That nervous and emotional strain is the immediate cause, precipitating the syndrome in susceptible individuals.

4. That in the cause of susceptibility (acquired instability of the autonomic nervous system) infection plays a predominant role and the susceptibility in such cases may be accepted as indicating a chronicity of the infection with constant or frequent outpourings into the blood of the infective agent.

5. That there is a certain rationale for believing that this instability in the autonomic nervous system lies in the element of anaphylaxis in disease in the predilection of anaphylatoxin for the parasympathetic system.

6. That there is some evidence that deficiencies of calcium in the diet may have played a part in the causation of some of the phenomena and that the higher plane of inorganic metabolism in the organism may have shared with adrenin increase the responsibility in causation of the thyroid hyperplasia and hyperthyroidism among the soldiers.

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THE RELATION OF THE BACILLUS INFLUENZA TO THE RECENT EPIDEMIC.

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As an indication of the comparative suddenness of this epidemic, it may be noted that in the index number of the *Journal of the American Medical Association*, June 29, 1918, which includes the preceding six months, there are but three references to influenza. During the following six months the index number of the same journal shows over 175. Yet in spite of the many articles on the subject, there still remain certain unanswered questions. One of these undetermined points is the source of the epidemic, another refers to the date of its inception, a third as to the etiological factor.

Naturally, no country is particularly anxious to admit that it was the originator of the outbreak, any more than in the past was there any desire to claim paternity for syphilis, which in France was known as the Italian disease, while in Italy it was accredited to France. Although the present infection has been known popularly as the "Spanish Flu," there is really very little incriminating evidence.

It seems that during the early spring, and also in the autumn of 1917, scattered cases of influenza were reported from as widely separated areas as England, France, Vienna and lower Austria. At no time did it reach epidemic proportions, yet the evidence indicates that the potential possibilities were present. During the winter of 1917 and 1918 there does not seem to have been any noticeable increase. In the middle of April, 1918, the reports from the A. E. F. showed, however, that a widespread outbreak had occurred of a disease whose course was characterized by a sudden onset, high fever, headache and backache, lasting three to five days, and leaving in most instances a profound weakness. This epidemic was of unusual mildness and disappeared largely by the end of July.